

## **REMARKS**

### **I. Amendments**

Claims 1, 2, 10, 23 and 27 have been amended in response to the Examiner's rejections. Claims 12 and 32 were canceled herein, claims 6-7, 13-16, 24-26, 34, 36-41, 43-44, 46 and 48 being canceled in a previous amendment. The Examiner has indicated that claims 4, 5, 8-12, 17-23, 27-33, 35, 42, 45 and 47 are allowed.

The amendments to the claims do not add or constitute new matter. Support for the amendments may be found throughout the specification and originally filed claims.

The foregoing amendments are made solely to expedite prosecution of the instant application, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicants reserve the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, claims 1-5, 8-11, 17-23, 27-31, 33, 35, 42, 45 and 47 are pending in the instant application.

### **II. Double Patenting**

The Examiner advised Applicants that should claim 12 be found allowable, claims 27 and 32 will be objected to under 37 C.F.R. § 1.75 as being substantial duplicates thereof. The Examiner has suggested that in the instant case, each of the claims is directed to a method limited to comprising the steps of administering an agent to the transgenic mouse of claim 8 and determining whether an eye abnormality of the transgenic mouse is ameliorated.

The Examiner's objection is no longer relevant as a result of the cancellation of claims 12 and 32. Of these claims, only claim 27 remains pending in the application.

### **III. Rejections**

#### ***A. Rejection under 35 U.S.C. § 112, second paragraph***

Claims 10 and 23 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse the rejection.

Specifically, the Examiner has asserted that the claims are indefinite for omitting essential steps, such omission amounting to a gap between steps. The Examiner argues that the omitted step is: selecting for a cell which has undergone homologous recombination. The Examiner suggests inserting this step after step (a) and prior to the step of introducing the cell into a blastocyst.

Further, the Examiner states that the claims are indefinite in their recitation of a “pseudopregnant mouse gives birth” in that a pseudopregnant mouse cannot give birth. The Examiner suggests reciting that “said pseudopregant mouse gives birth.”

Applicants disagree with the Examiner’s conclusions. However, in order to expedite prosecution, Applicants have adopted the Examiner’s suggested modifications. Therefore the rejection is no longer relevant, and withdrawal of the rejection is respectfully requested.

***B. Rejection under 35 U.S.C. § 102***

The Examiner has rejected claims 1 and 3 under 35 U.S.C. § 102(b) as being anticipated by Qin *et al.* (1992) *J. Biol. Chem.* 267:8458-8463. Applicants respectfully traverse the rejection.

Qin *et al.* is cited by the Examiner as teaching a nucleic acid construct comprising a cGMP phosphodiesterase gene and a selectable marker and a method of making the construct. The Examiner argues that these claims read on any nucleic acid comprising a cGMP phosphodiesterase and selectable marker because the selectable marker can be anywhere in the construct and the two sequences are not limited to being non-contiguous.

Applicants disagree that the Qin reference anticipates each and every limitation of the pending claims. However, in order to expedite prosecution of the application, Applicants have amended the claims. The amended claims now recite the location of the selectable marker. Applicants note that the Qin reference does not teach or disclose a nucleic acid construct wherein the selectable marker is located between the first and second sequences homologous to the cGMP phosphodiesterase gene. As such, withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-849.

Respectfully submitted,

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